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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,065	KIPP ET AL.	
	Examiner	Art Unit	
	David H Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *1,3,7,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-6,8-16 and 19-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8 July 2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 2, 4-6, 8-16 and 19-37 in the reply filed on 30 March 2004 is acknowledged. The requirement to elect one nucleotide sequence in conjunction with Group II is herein withdrawn, SEQ ID NO: 1 encoding SEQ ID NO: 2 and SEQ ID NO: 3 encoding SEQ ID NO: 4 will be examined together in view of the over 99% similarity between SEQ ID NO: 1 and SEQ ID NO: 3.

2. Claims 1, 3, 7, 17 and 18 are withdrawn from further consideration pursuant to 37 CFR § 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 30 March 2004.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17(i).

Information Disclosure Statement

4. The information disclosure statements filed 8 July 2002 has been considered, a signed copy is attached hereto.

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR § 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: Non-initialed and/or non-dated alterations have been made to the oath or declaration filed 28 May 2002 by Inventor Tong Zhu. See 37 CFR § 1.52(c).

Drawings

6. The Examiner accepts the drawing(s) filed 20 December 2001.

Specification

7. The Specification is objected to because the incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper (see page 28, lines 27-28, page 33, line 7, page 36, lines 15-16, page 39, line 4, page 55, line 13 and page 62, lines 6-9). Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Sequence Rules

8. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1)

and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825. Specifically, page 43, line 30 "MWLQP" and page 52, line 2 "DYYT", of the Specification. Applicant must submit a CRF copy and paper copy of the Sequence Listing, a statement that the content of the paper and computer readable copies are the same and where applicable include no new matter as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(d), as well as an amendment directing its entry into the specification. Alternatively, if these amino acid sequences lie within one of the disclosed sequences, amendment to the specification to indicate their location in a disclosed sequence would suffice.

Failure to comply with these requirements in response to this Office Action will result in ABANDONMENT of the application under 37 CFR § 1.821(g).

Claim Objections

9. Claim 29 is objected to under 37 CFR § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This claim does not appear to further limit the method of claim 26, said claim appears to be directed to an inherent property of the method of claim 26.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 2, 4-6, 9-16 and 19-37 rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At claim 2(g), line 1, "stringent conditions" renders the claim indefinite because the teachings of the specification only gives general guidance and does not teach the metes and bounds of the claimed nucleic acid (see pages 13-14 of the specification).

At claim 2(h), lines 1 and 3, "or variant of" renders the claim indefinite because the specification does not teach the metes and bounds of the claimed nucleic acid (see page 8, 2nd paragraph of the specification).

At claim 4, line 2, "nucleotide sequence" lacks proper antecedent basis in claim 2 directed to an isolated nucleic acid molecule.

At claim 9, line 3, "nucleotide molecule" lacks proper antecedent basis in claim 2 directed to an isolated nucleic acid molecule.

At claim 16, line 3, "nucleotide molecule" lack proper antecedent basis in claim 2 directed to an isolated nucleic acid molecule.

At claim 19, line 2, "nucleotide molecule" lack proper antecedent basis in claim 2 directed to an isolated nucleic acid molecule.

At claim 20, line 1, "said nucleotide construct" lacks proper antecedent basis in claim 19. At line 3, "said nucleotide sequence" lacks proper antecedent basis in claim 19 and should read – nucleic acid molecule --. See also claim 21, line 2.

Claim 24 is indefinite because it is unclear if an additional method step is intended or if the introducing method step at claim 19 is being further limited, hence the metes and bounds of the claim are unclear.

Claim 25 is indefinite because it is unclear if an additional method step is intended or if the introducing method step at claim 19 is being further limited, hence the metes and bounds of the claim are unclear.

Claim 26 is indefinite because at line 2, "nucleotide sequence" denotes information and not a composition of matter, hence it is unclear what the metes and bounds of the claimed method are. Amending the claim to read -- nucleic acid molecule comprising a nucleotide sequence -- would obviate this rejection, and would be consistent with claim 2. See the Federal Register, Vol. 66, No. 4, January 5, 2001, page 1095, center column, comment No. 13. See also claim 30, line 2

At claim 26(g), line 1, "stringent conditions" renders the claim indefinite because the teachings of the specification only gives general guidance and does not teach the metes and bounds of the claimed nucleic acid (see pages 13-14 of the specification).

At claim 26(h), lines 1 and 3, "or variant of" renders the claim indefinite because the specification does not teach the metes and bounds of the claimed nucleic acid (see page 8, 2nd paragraph of the specification).

Claim 28 is indefinite because it is unclear if an additional method step is intended or if the method step if introducing at claim 26 is being further limited hence the metes and bounds of the claim are unclear.

Claim 34 is indefinite because it is unclear if this claim is directed to an additional method step or is further limiting the introducing step at claim 26, hence the metes and bounds of the claim are unclear.

Claim 35 is indefinite because it is unclear if this claim is directed to an additional method step or is further limiting the introducing step at claim 26, hence the metes and bounds of the claim are unclear.

At claim 36, line 2, "nucleotide molecule" lack proper antecedent basis in claim 2 directed to an isolated nucleic acid molecule.

At claim 37, line 3, "nucleotide sequence" lacks proper antecedent basis in claim 36 and should read -- nucleic acid molecule --.

Those claims not specifically addressed in this rejection are deemed indefinite because they do not obviate the indefiniteness of the claim(s) upon which they depend.

12. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 2, 4-6, 9-16 and 19-37 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims an isolated nucleic acid molecule comprising a nucleotide sequence (1) at least 85% identical to SEQ ID NO: 1 or 3; (2) comprising at least 50

contiguous nucleotides of SEQ ID NO: 1 or 3; (3) that hybridizes under stringent conditions to a nucleotide having the nucleotide sequence of SEQ ID NO: 1 or 3; and (4) encoding a fragment or variant of the amino acid sequence of SEQ ID NO: 2 or 4 that confers a dominant-negative phenotype in a host cell. Applicant also claims a method of altering recombination frequency in a plant comprising introducing such nucleic acid molecule and plants transformed to comprise said nucleic acid molecule.

Applicant describes SEQ ID NO: 1 encoding SEQ ID NO: 2 and SEQ ID NO: 3 encoding SEQ ID NO: 4, both nucleic acid molecules encoding a tobacco MSH2 protein involved in mismatch repair. Applicant also describes a 265 amino acid, N-terminal fragment of said MSH2 protein with produces a mutator phenotype when expressed in *E. coli* (Example 5, pages 51-52 of the specification).

Applicant does not describe the genus of nucleic acid molecules comprising a nucleotide sequence (1) at least 85% identical to SEQ ID NO: 1 or 3; (2) comprising at least 50 contiguous nucleotides of SEQ ID NO: 1 or 3; (3) that hybridizes under stringent conditions to a nucleotide having the nucleotide sequence of SEQ ID NO: 1 or 3; or (4) encoding a fragment or variant of the amino acid sequence of SEQ ID NO: 2 or 4 that confers a dominant-negative phenotype in a host cell.

Hence, it is unclear from the instant specification that Applicant was in possession of the invention as broadly claimed.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an

adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. At 1406, the court states that a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. See also, MPEP § 2163 which states that the claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

14. Claims 2, 4-6, 9-16 and 19-3 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 3, or encoding a fragment encoding residues 1-266 thereof, and methods of using said isolated nucleic acid molecule, does not reasonably provide enablement for an isolated nucleic acid molecule comprising a nucleotide sequence (1) at least 85% identical to SEQ ID NO: 1 or 3; (2) comprising at least 50 contiguous nucleotides of SEQ ID NO: 1 or 3; (3) that

hybridizes under stringent conditions to a nucleotide having the nucleotide sequence of SEQ ID NO: 1 or 3; and (4) encoding a fragment or variant of the amino acid sequence of SEQ ID NO: 2 or 4 that confers a dominant-negative phenotype in a host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant claims an isolated nucleic acid molecule comprising a nucleotide sequence (1) at least 85% identical to SEQ ID NO: 1 or 3; (2) comprising at least 50 contiguous nucleotides of SEQ ID NO: 1 or 3; (3) that hybridizes under stringent conditions to a nucleotide having the nucleotide sequence of SEQ ID NO: 1 or 3; and (4) encoding a fragment or variant of the amino acid sequence of SEQ ID NO: 2 or 4 that confers a dominant-negative phenotype in a host cell. Applicant also claims a method of altering recombination frequency in a plant comprising introducing such nucleic acid molecule and plants transformed to comprise said nucleic acid molecule.

Applicant teaches SEQ ID NO: 1 encoding SEQ ID NO: 2 and SEQ ID NO: 3 encoding SEQ ID NO: 4, both nucleic acid molecules encoding a tobacco MSH2 protein involved in mismatch repair. Applicant also teaches a 265 amino acid N-terminal fragment of said MSH2 protein with produces a mutator phenotype when expressed in *E. coli* (Example 5, pages 51-52 of the specification).

Applicant does not teach nucleic acid molecule comprising a nucleotide sequence (1) at least 85% identical to SEQ ID NO: 1 or 3; (2) comprising at least 50 contiguous nucleotides of SEQ ID NO: 1 or 3; (3) that hybridizes under stringent

conditions to a nucleotide having the nucleotide sequence of SEQ ID NO: 1 or 3; or (4) encoding a fragment or variant of the amino acid sequence of SEQ ID NO: 2 or 4 that confers a dominant-negative phenotype in a host cell.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

The art of making and using nucleic acid molecules that encode mismatch repair proteins, in particular MSH2 proteins, to which the instant invention is directed, is complex. MSH2 proteins are one member of a protein complex involved in identifying and repairing DNA mismatches during replication. A MSH2 protein binds to a MSH6 protein and an ATP molecule, after which a MLH1 and PMS1 protein heteroduplex binds to the MSH2 and MSH6 heteroduplex (Bowers *et al* 2000, J. Mol. Biol. 302:327-338, see Figure 7 on page 335). Given this type of association, MSH2 proteins comprise multiple and complex-binding regions on the protein involved in their function. Applicant has provided limited guidance on how to make and use nucleic acid molecules that encode fragments and variants of the exemplified tobacco MSH2 proteins, or fragments of said nucleic acid molecules as broadly claimed. Pang *et al* (1997, Molecular and Cellular Biology 17(8): 4465-4473) teach that a yeast Pms1p

(amino acids 1-271) truncation mutation, yeast Pms1p being the functional equivalent of the mammalian PMS2, did not have a dominant negative effect (see Table 1 on page 4470). In addition, it has been found that the dominant-negative phenotype in the *E. coli* MutL protein appears to be associated with the conserved N-terminal portion of the MutL protein, and that the dominant-negative phenotype requires a high level of expression (see page 4472, left column, 3rd paragraph). Thus, the art teaches that it is unpredictable whether a truncated to modified mismatch repair protein will actually affect MMR function in a cell without empiric evidence.

It cannot be predicted by one of skill in the art that nucleic acids that are at least 85% identical will encode a protein with the same activity as either SEQ ID NO: 1 or 3. Bowie *et al* (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie *et al* teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The

sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252), who teach that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect, but that replacement with serine or glutamic acid sharply reduced biological activity (see the abstract), and that substituting Leu-48 for Ile produced a product with unexpectedly very low activity (see page 1251, left column, last paragraph). Small changes in amino acid sequence can completely modify enzymatic function. Broun *et al* (1998, Science 282:1315-1317) teach that a change of four amino acids converts an oleate 12-desaturase to a hydroxylase. Thus, Lazar *et al* and Broun *et al* demonstrated that one or few amino acid substitutions could dramatically affect the biological activity and the structure-function characteristics of a protein in unpredictable ways.

Claim 21, 24 and 26-37, directed to methods of using an antisense nucleotide sequence, or cosuppression, are deemed to only be enable to the extent that they are directed to a method in tobacco because the use of antisense suppression using an antisense construct or cosuppression in a heterologous plant is an unpredictable art due to the requirement of complementation of the expressed message in the plant cell to suppress expression of a protein encoding nucleic acid. Applicant provides no working examples of antisense suppression or cosuppression of a MSH2 protein in a plant, and only general guidance (page 24, 2nd paragraph of the specification). The art teaches that suppression of expression of heterologous sequences using an antisense construct is not predictable. Colliver *et al* (1997, Plant Molecular Biology 35:509-522) teach that

expressing an antisense chalcone synthase gene from *Phaseolus vulgaris* in the plant *Lotus corniculatus* did not predictable suppress expression of the heterologous gene, and in some cases increased expression of the endogenous gene (see abstract). Elomaa *et al* (1996, Molecular Breeding 2:41-50) teach that expression of an antisense construct of a chalcone synthase gene gchs1 or gchs2, which are 73% identical to each other, do not cross suppress expression of the endogenous genes, in fact overexpression of the antisense gchs1 gene had no suppressive effect (see pages 47-49).

Claims 25 and 28 directed to methods using chimeraplasty lack adequate enablement. Applicant provides only generalized guidance on how to make and use nucleotide constructs to practice this type of method (page 36, 2nd paragraph of the specification). Applicant provides no working examples of using chimeraplasty to produce a plant having altered recombination frequency as broadly claimed. The art teaches that using chimeraplasty to modify a coding sequence is not predictable. Andersen *et al* (2002 J. Mol. Med. 80:770-781) teach that in plants mixed base sequences other than the predicted nucleotide conversion have been observed suggesting a plant-specific repair mechanism different from that found in mammalian systems, and that the mechanisms underlying this type of gene conversion are not fully understood (page 772, right column). Andersen *et al* also teach that the efficiency of the gene correction process may furthermore be influenced by the differential recognition of mismatches by repair enzymes and possible sequence context effects (page 770, right column). Liu *et* al (2003, Nature Reviews Genetics 4:679-689) that

although the list of successful targets using chimeraplasty is extended monthly, the variable levels of correction frequency continue to baffle investigators and that this frustrating variability has been the subject of much correspondence to scientific journals, some of which points out persistent failures to achieve any detectable correction (page 682, right column, 3rd paragraph).

Hence, given Applicant's limited guidance on how to make and use variants of the exemplified nucleic acid molecules or variants of the encoded proteins, how to make and use other nucleic acids that hybridize under stringent conditions, how to use 50 nucleotide base pair fragments of the exemplified nucleic acid molecules, and how to make and use nucleic acids encoding variants of the exemplified, encoded MSH2 proteins it would have required undue trial and error experimentation by one of skill in the art at the time of Applicant's invention to practice the invention as broadly claimed. In addition, those claims directed to antisense suppression or cosuppression, or to chimeraplasty techniques, such methods are deemed unpredictable was broadly claimed and would have required undue trial and error experimentation or practice the methods. See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970) which teaches "That paragraph (35 USC § 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases

involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.".

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claim 2 is rejected under 35 U.S.C. § 102(b) as being anticipated by Culligan and Hays (June 2000, The Plant Cell, 12:991-1002).

Culligan and Hays disclose isolated nucleic acids encoding a Arabidopsis thaliana and a Zea mays MSH2 protein, that would bind under "stringent conditions" to a nucleic acid having the sequence of either of Applicant's SEQ ID NO: 1 or SEQ ID NO: 3. Said isolated nucleic acids would also be considered to encode variants of the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 4. Hence, Culligan and Hays have previously disclosed the claim limitations.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 4-6, 9-16, 19, 20, 22, 23, 26-27, 29-33, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chao *et al* (US-PGPUB US 2003/0143286 A1, filed 11 October, 2002 which claims benefit of Provisional Application 60/328,750 filed 12 October 2001). Provisional Application 60/328,750 is attached hereto.

Chao *et al* teach a method of making a plant transformed with an isolated nucleic acid encoding an AtMSH2 protein that operates as a dominant negative allele in the plant (see claim 11, and page 9 at ¶ 0081). Chao *et al* teach that said method can be used to make transgenic *Brassica* sp. or monocot plants (page 5, ¶ 0051). Chao *et al* teach such a dominant negative allele can comprise a truncation mutation of a mismatch repair protein (page 8, ¶ 79). The *Arabidopsis thaliana* MSH2 encoding nucleic acid would have been considered capable of hybridizing under stringent conditions with the nucleic acid of Applicant's SEQ ID NO: 1 or 3 (SEQ ID NO: 46).

Chao *et al* do not specifically teach plants transformed with a MSH2 dominant negative allele or constructs to make such.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to use the teachings of Chao *et al* to make an expression cassette comprising the AtMSH2 encoding nucleic acid or a truncation thereof, operably linked to a plant operative promoter and transform a plant, wherein said plant has increased recombination frequency and an altered DNA repair process. The plants taught by Chao *et al* would have been viewed by one of ordinary skill in the art to be functional equivalents and would not have lead to a teaching of unexpected results as to the particular plant transformed.

Conclusion

19. Claims 21, 24, 25, 28, 34 and 35 are free of the prior art, which neither teaches nor fairly suggests using antisense suppression, cosuppression or chimeraplasty of a plant MSH2 encoding nucleic acid to alter DNA repair processes.

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (571) 272-0804. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (571) 272-0547.

David H. Kruse
AU 1638

David H. Kruse, Ph.D.
10 June 2004